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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/731,816	12/08/2000	Reinhard Ebner	PF470P1	1781

22195 7590 12/27/2002

HUMAN GENOME SCIENCES INC
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EXAMINER
SPECTOR, LORRAINE

ART UNIT	PAPER NUMBER
1647	10

DATE MAILED: 12/27/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	Examiner	Group Art Unit	

---The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address---

Period for Response

A SHORTENED STATUTORY PERIOD FOR RESPONSE IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a response be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for response specified above is less than thirty (30) days, a response within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for response is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to respond within the set or extended period for response will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☒ Responsive to communication(s) filed on 10/10/02.

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☒ ~~Claim~~(s) 50-103 is/are pending in the application.

Of the above claim(s)_____ is/are withdrawn from consideration.

☐ Claim(s)_____ is/are allowed.

☒ ~~Claim~~(s) 50-103 is/are rejected.

☐ Claim(s)_____ is/are objected to.

☐ Claim(s)_____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on_____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on_____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number)_____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received:_____.

Attachment(s)

☒ ~~In~~formation Disclosure Statement(s), PTO-1449, Paper No(s). 13

☐ Interview Summary, PTO-413

☒ Notice of References Cited, PTO-892

☐ Notice of Informal Patent Application, PTO-152

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Other_____

Office Action Summary

Part III: Detailed Office Action

Claims 50-103 are pending and under consideration.

Formal Matters:

The disclosure is objected to because of the following informalities: It is noted that the specification refers to the protein of SEQ ID NO: 4 as Interleukin-22. However, it is noted that, while applicant may be their own lexicographer, the nucleic acid of SEQ ID NO: 3 does not encode the protein which has attained recognition in the art as being Interleukin-22, as set forth in the previous Office Action. If applicants wish to continue to refer to their protein as IL-22, they should amend the specification to clearly indicate that this protein is not the same as the protein known by the art-accepted designation IL-22. As this problem was identified in the first office action on the merits, delay of correction until after allowance of claims, which correction may be extensive, will not be considered to be timely.

Appropriate correction is required.

The information disclosure statement filed 10/10/02 has been considered. References AH-BX are Genbank Accession numbers and have been considered *only* insofar as the printed, non-sequence information is concerned. The relevance of the actual sequences themselves to the claimed subject matter cannot be assessed in the absence of either a statement or relevance or an alignment to SEQ ID NO: 4.

Objections and Rejections under 35 U.S.C. 112:

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 50-103 remain rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility

for reasons cited in the previous Office Action, paper number 10 mailed 6/10/02, at page(s) 2-6. Applicants arguments in paper number 12, filed 10/10/02, have been fully considered but are not deemed persuasive.

Applicants argue that the citations by the Examiner in the previous Office action are not germane to interleukins (page 5 of paper number 12) has been fully considered but not deemed persuasive. The cited art demonstrates the level of predictability in the art, using other cytokines. Applicants argument presumes that "interleukins" are somehow related structurally, and more related to each other than to other cytokines, which is not the case. Cytokines may be grouped by biological function (i.e. the effect on the organism), by the structure of the receptor to which they bind, by specific structural motifs in the cytokines themselves, or by what chromosome encodes them, among other properties. Contrary to applicants assertions of similarity to IL-17 and IL-20, there was no significant overall homology to IL-17 when the sequence search for this case was performed (i.e. IL-17 was not returned as a 'hit'; IL-20 was not yet publicly available), and the short, limited motifs listed at pages 14-16 of the specification are not associated with any particular functions. Therefore, while indicating some *potential* evolutionary relatedness to IL-17, such are not predictive of function. Identity with IL-20 cannot be assessed, as such is not publicly available. Therefore, not conclusions regarding activity can be made with respect to IL-20. The issue here is not, as stated by applicants at page 5 that "IL-22 of the present invention cannot have similar biological functions as its homologs, i.e. IL-17 or IL-20", but rather that one of skill in the art would not accept the assertion that IL-22 (as identified herein) has the same activity of IL-17 or IL-20 based upon the sketchy information proffered in the specification, including the absence of relevant biological data.

At page 6, applicants argue that genomic annotations are a valid and successful tool. This argument has been fully considered but is not deemed persuasive because, while true, that such are useful tools, it is *not* true that one of ordinary skill in the art would accept an assignment of biological function based upon such annotations; the standard in the art is to use such annotations as 'leads' of possible functions, and then to follow up those leads by actual experimentation.

According to the Cytokine FactsBook 2nd edition, (Academic Press, 2001), IL-17 "is a T

cell-derived cytokine that does not act directly on haematopoietic cells but stimulates stromal cell elements (epithelial cells, endothelial cells and fibroblasts) to secrete cytokines including IL-6, IL-8, G-CSF and prostaglandin E2." However, the specification discloses the activity of IL-22 on NIH-3T3 cells, which are mouse fibroblast-type cells, only as "modulating" IL-6 production. There is no disclosure of whether such modulation is positive or negative, nor under what conditions, nor that it shares any other function with IL-17, specifically induction of other cytokines. As evidence by the prior art cited in the previous Office Action, even closely related cytokines can have opposing functions. Therefore, the disclosure of limited, localized similarity to IL-17, taken with the indefinite disclosure that IL-22 "modulates" IL-6 production by NIH-3T3 cells is not a clear indication that IL-22 induces such production, and therefore does not clearly confer utility to the protein, nor the antibodies that bind to it.

At page 8, applicants argue that immunophenotyping is a sufficient utility under 35 U.S.C. § 101. This argument has been fully considered but is not deemed persuasive. As stated in the previous Office Action, use for "immunophenotyping" is not considered by the Patent Office to be a specific or substantial utility, as such use could be asserted for *any* naturally occurring protein, and further because there has been no characterization of the expression of the disclosed IL-22.

Finally, it is noted that applicants refer repeatedly to the "interleukin(s) superfamily". The Examiner notes that there is no such recognized "superfamily" in the art. Proteins are called interleukins for various reasons; while all are cytokines, they are not considered to comprise a single 'superfamily', but rather are relegated to various *different* cytokine families, along with other cytokines. As stated The Cytokine FactsBook, 2nd ed., at page 3, "It should become clear from reading the entries in this book that cytokine nomenclature owes little to any systematic relationships between molecules. This is a reflection of the different historical approaches to naming new cytokines which

were based either on cell of origin or initial defining bioassay. These systems have created anomalies such as tumour necrosis factor, originally defined as causing necrosis of solid tumours, but which is now thought to be primarily an immunomodulatory and proinflammatory cytokine, and which has

proven ineffective as an anticancer agent in several clinical trials. The interleukin nomenclature, which merely assigns a sequential number to new factors, is a rational system, but it has not been universally applied to new factors. A consensus on the grouping of cytokines into families has settled on classifying cytokines based on the structure of their receptors." Thus, the interleukins are merely sequentially numbered cytokines, which numbers are assigned without regard to structure or function. At page 4 of The Cytokine FactsBook, 2nd ed., it can further be seen that by the current grouping of cytokines according to the structure of their receptors, the interleukins fall into all groups except TNF receptors and tyrosine kinase receptors, and *IL-17 does not fall into any of the recognized families.*

Accordingly, it remains that the instant claims are drawn to antibodies which bind a protein which has undetermined function or biological significance, and cells which produce such. Until some actual and specific activity can be attributed to the protein identified in the specification as IL-22 protein or the antibodies that bind to it, the claimed invention is incomplete, and lacks utility under 35 U.S.C. § 101.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 50-103 also remain rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. Applicants traversal of this rejection is not persuasive for reasons cited with respect to the rejection under 35 U.S.C. § 101, above.

Claims 77-103 are further rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The deposit of biological organisms is considered by the Examiner to be necessary for enablement of the current invention (see 37 C.F.R.§1.808(a)). Examiner acknowledges the deposit of organisms under accession number ATCC209665 under terms of the Budapest Treaty on International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure in partial compliance with this requirement. However, in order to be fully compliant with the requirement, applicants must state that all restrictions on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent. See 37 C.F.R.§1.808(a)(2). Applicants attempt to comply with this requirement is noted, however applicants fail to specifically refer to the deposit, i.e. ATCC 209665.

Claims 51, 67, and 77-103 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims which recite that the protein to which the claimed antibodies bind is glycosylated, e.g. claims 51, 67, 78, and 94 are not supported by the specification because there is no description of any glycoslyation of the protein represented by SEQ ID NO: 4 residues 1-160. While it is possible that the protein is glycosylated, there is no description of such. It is not predictable where or how a protein will be glycosylated, and in what host cell systems such glycosylation will occur. While it is possible that glycosylation can affect the immunogenicity of a protein, such is also not predictable. Therefore, with respect to antibodies that would bind specifically to a glycosylated form of the protein (as opposed to a non-glycosylated form of the protein) there is no written description of such glycosylation, and therefore of the antibodies that would bind to such. A mere conjecture

that the protein might be glycosylated under some unspecified conditions is not sufficient to describe antibodies that bind to such a glycosylated protein. Applicants traversal of this rejection has been fully considered but is not deemed persuasive. Applicants argue that potential glycosylation sites are identified in the specification, see page 9 of paper number 12. This argument has been fully considered but is not deemed persuasive because *potential* glycosylation sites are not predictive of actual glycosylation *in vivo*. While such sites are necessary for glycosylation, it remains unpredictable in the art whether or not glycosylation will actually take place at such a site. Accordingly, identification of such is not conception of whether or not the protein is actually glycosylated at such a site. Further, 'glycosylation' is not a single type of modification; glycosylation groups may differ substantially in structure and function. Thus it remains that no actual glycosylation of the protein has been described, nor have any antibodies that would bind preferentially to the glycosylated form of the protein. The Examiner notes applicants citations of the revised written description guidelines, and maintains that in this case, the mere statement that glycosylated forms of the protein are included in the invention, there is no conception of whether such glycoslyation actually occurs, at which, if any, of the identified sites, nor what the nature of such glycosylation might be, including whether or not such glycosylation would affect the breadth of the claims (i.e. whether there would exist any antibodies that would bind the glycosylated vs. the non-glycosylated form of the protein, or vice versa). Thus, in this case, the finding that conception does not occur until there is a reduction to practice, i.e. until the actual glycosylation of the protein is characterized, is appropriate. Contrary to applicants argument at page 12, no crystalline structures of the protein are required; all that would be required would be a demonstration that the protein actually becomes glycosylated, and that such is of a nature that one of ordinary skill in the art would consider it reasonably predictable that there would be a difference in scope between claims that bind to the protein and claims that bind to glycosylated form(s) of the protein. Accordingly, it remains that only antibodies which bind to the unmodified protein of SEQ ID NO: 4, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph.

Claims drawn to antibodies which bind a protein encoded by a deposited plasmid, i.e. claims 77-103, also lack adequate written description. At page 9, paragraph 1 of the specification, it is stated that "a representative clone containing all or most" ... "of the sequence for SEQ ID NO: 3 was deposited". It is not clear what has been deposited, of what it encodes. "All or most" is not an adequate written description of the deposited material. Applicants citation of the decision in *Enzo Biochem, Inc. v. Gen-Probe* is noted. However, as the deposit in question does not yet meet the public availability requirement, such is not persuasive.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 51, 67, 78 and 94 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 51, 67, 78 and 94 are indefinite because it is not clear how the glycosylation state of the protein affects the claimed antibodies, both because it is not predictable that glycosylation will change the antigenic structure of the protein, and because there is no written description of such glycosylation, such that the metes and bounds of the claims cannot be determined. Applicants traversal of this rejection has been fully considered but is not deemed persuasive for reasons cited above.

The remaining claims are rejected for depending from an indefinite claim.

Prior Art:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 50, 51, 53-58, 61-65, 67, 77, 78, 80-85, 88, 89, 90, 92, 94, 96-100 and 103 remain rejected under 35 U.S.C. 102(b) as being anticipated by Sutcliffe, U.S. Patent Number 5,242,798 for reasons set forth in the previous Office Action at pages 9-10.

Applicants traversal of this rejection has been fully considered but is not deemed persuasive. Applicants citation of a portion of the rejection under 35 U.S.C. § 103(a) over the same reference in traversal of this rejection is moot, as the monoclonal antibody, cell and hybridoma claims are not rejected under 35 U.S.C. § 102(b). Applicants also traverse that an antibody that binds to Sutcliffe's P2 peptide would not specifically bind to a protein of SEQ ID NO: 4 or encoded by ATCC 209665, but fail to provide rationale, reasoning or evidence to support such an assertion. The art-accepted definition of 'specific' binding would not preclude such, and the claims and specification do not provide a definition that would preclude such.

It is noted that applicants have neither confirmed nor denied that the deposited strain encodes SEQ ID NO: 4.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 59, 60, 66-67, 69-76, 86, 87, 91, 93, 101 and 102 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Sutcliffe, U.S. Patent Number 5,242,798 in view of Coughlin, U.S. Patent Number 5,256,766 for reasons set forth in the previous Office Action at pages 10-11. Applicants arguments have been fully considered but are not deemed persuasive for reasons cited above with respect to the rejection under 35 U.S.C. § 102(b).

Claims 50-103 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bonaldo et al., locus HUMNOTIA in view of Sibson et al., WO94/01548 for reasons set forth in the previous Office Action at pages 11-12. Applicants arguments have been fully considered but are not deemed persuasive. Applicants argue that "no standard features, such as an open reading frame, are not disclosed or evident" from Bonaldo's sequence. This argument has been fully considered but is not deemed persuasive because Bonaldo's sequence is clearly identified as being from cDNA, which the person of ordinary skill in the art would know is transcribed from a gene as mRNA, which is translated to produce protein. Further, the teachings of Sibson et al. pertain to just such cDNA sequences, and clearly indicate that one of ordinary skill in the art would both expect an open reading frame to be present, and know how to locate such; see for example page 8, paragraphs 3-4, with specific reference to antibodies in paragraph 5. Further, as Sibson's disclosure pertains to nucleic acid fragments from brain, and Bonaldo's cDNA is from brain, motivation would seem to be clearly provided by the Sibson disclosure.

Advisory Information:

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Lorraine M. Spector, whose telephone number is (703) 308-1793. Dr. Spector can normally be reached Monday through Friday, 9:00 A.M. to 5:30 P.M.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached at (703)308-4623.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist at telephone number (703) 308-0196.

Certain papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Examiner Spector via telephone number 703-746-5228. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Lorraine Spector, Ph.D.
Primary Examiner

LMS
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